

October 23, 1958

Dr. Fred Karush
Childrens Hospital
1740 Bainbridge Street
Philadelphia 46, Pa.

Dear Fred:

I was just delighted to get that last reprint from you entitled "Structural and Energetic Aspects of Antibody Hapten Interactions". That experiment with urea is one I was proposing to Harold Deutsch just the other day and neither of us had been aware that you had already done it. The result you got was what I would have considered in advance to be strong confirmatory evidence that antibody sequence does depend on just such structural factors as sequence of amino acids. If I can reconstruct your reasoning your main argument against sequence is the lack of a plausible mechanism for instruction of sequence by an antigen. Of course I agree with you wholeheartedly on this point and in fact this argument underlies my agreement with the conception that the antigen must have an elective or retrospective role in determining antibody specificity. Of course the structural factor would by no means whatsoever minimize the role of disulfide linkages in holding the protein together and determining its essential shape but I would consider that the possible configurations that disulfide linkages could establish would depend on sequence considerations.

Now what I would like to press you for an answer on is whether there are any other compelling arguments against the differentiation of antibodies on the basis of amino acid sequence.

With best regards.

Yours sincerely,

Joshua Lederberg
Professor of Medical Genetics

JL/jp